Health Advisory:

Evaluation and Reporting of Suspected Cases of Avian Influenza A (H5N1)

February 18, 2004

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Health Advisory
February 18, 2004

FROM: **RICHARD C. DUNN**
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SUBJECT: **Recommendations for Evaluation and Reporting of Suspected Cases of Avian Influenza A (H5N1)**

During December 2003 - February 2004, outbreaks of highly pathogenic avian influenza A (H5N1) among poultry were reported in Cambodia, China, Indonesia, Japan, Laos, South Korea, Thailand, and Vietnam. As of February 18, 2004, a total of 31 cases of laboratory-confirmed influenza A (H5N1) virus infections in humans, resulting in 22 deaths, has been reported in Thailand and Vietnam. In addition, a number of suspected cases in humans are under investigation by national health authorities in Thailand and Vietnam.

The majority of the human H5N1 cases are apparently associated with direct exposure to infected birds or to surfaces contaminated with excretions from infected birds. While no evidence for sustained person-to-person transmission of influenza A (H5N1) has been identified, previous experiences with avian influenza viruses suggest that limited person-to-person transmission of the current H5N1 viruses could occur. In addition, influenza viruses have the capacity to change quickly. Although no evidence of genetic reassortment between avian H5N1 viruses and human influenza viruses has been identified, if such reassortment were to occur, the likelihood that the H5N1 virus could be transmitted more readily from person to person would increase. Continued monitoring for new transmission patterns is an important aspect of the current investigation, and the Centers for Disease Control and Prevention (CDC), the World Health Organization (WHO), and national health authorities in Asian countries are continuing to assess and monitor the situation. It is important to note that there have been no avian or human cases of influenza A (H5N1) reported in the United States.

This Health Advisory provides recommendations from CDC for medical providers and laboratories regarding influenza A (H5N1) surveillance, diagnosis, and testing. The final page summarizes information (as of February 9, 2004) about the human infections and avian outbreaks in Asia.

Suspected cases of influenza A (H5N1) should be reported immediately to the local public health agency, or the Missouri Department of Health and Senior Services at 800/392-0272 (24 hours a day – 7 days a week). More information on avian influenza is found on CDC's influenza web site at http://www.cdc.gov/flu/. Specific questions on avian influenza should be directed to Dr. Howard Pue, State Public Health Veterinarian, at PueH@dhss.mo.gov, or 573/751-6141.

Note that this Health Advisory pertains to influenza A (H5N1), which has caused disease in both birds and humans in Asia. It does not pertain to influenza A (H7N2) and influenza A (H2N2), which have recently caused infection in poultry, but not humans, in the northeastern United States. These latter avian influenza strains detected in the U.S. are different from the H5N1 strain causing disease in Asia, and they are believed to have low pathogenicity and to pose a low risk to humans.

Interim Recommendations for U.S. Surveillance and Diagnostic Evaluation[1]

The Centers for Disease Control and Prevention (CDC) recommends that state and local health departments, hospitals, and clinicians enhance their efforts to identify patients who could be infected by influenza A (H5N1) virus and take infection-control precautions (described in the figure below) when influenza A (H5N1) is suspected.

Interim recommended infection-control precautions* for influenza A (H5N1)

- All patients with a febrile respiratory illness should be asked about their recent travel history and managed using *Respiratory Hygiene/Cough Etiquette in HealthCare Settings* guidelines†.
- Isolation precautions for all hospitalized patients who have or are under evaluation for influenza A (H5N1) are the same as those that should be used for severe acute respiratory syndrome (SARS), as follows:
  - — Pay careful attention to hand hygiene before and after all patient contact.
  - — Use gloves and gown for all patient contact.
  - — Wear eye protection when within 3 feet of the patient.
  - — Place the patient in an airborne isolation room (i.e., monitored negative air pressure in relation to surrounding areas with six to 12 air changes per hour).
  - — When entering the patient's room, use a fit-tested respirator at least as protective as an N95 filtering-facepiece respirator approved by the National Institute for Occupational Safety and Health.
- Outpatients or hospitalized patients discharged in <14 days should be isolated in the home setting on the basis of principles for home isolation of SARS patients§.
- These precautions should be continued for 14 days after onset of symptoms until an alternative diagnosis is established or diagnostic test results indicate that the patient is not infected with influenza A virus.

* Additional information about health-care isolation precautions is available at http://www.cdc.gov/ncidod/hip/isolat/isolat.htm.
† Available at http://www.cdc.gov/flu/professionals/infectioncontrol/resphygiene.htm.
§ Available at http://www.cdc.gov/ncidod/sars/guidance.

Testing of hospitalized patients for influenza A (H5N1) infection is indicated when both of the following exist:

1. Radiographically confirmed pneumonia, acute respiratory distress syndrome (ARDS), or other severe respiratory illness for which an alternative diagnosis has not been established, and
2. A history of travel within 10 days of symptom onset to a country with documented H5N1 avian influenza infections in poultry or humans. Ongoing listings of countries affected by avian influenza are available from the World Organization for Animal Health at http://www.oie.int/eng/en_index.htm.

Testing for influenza A (H5N1) also should be considered on a case-by-case basis in consultation with state and local health departments for hospitalized or ambulatory patients with all of the following:

1. Documented temperature of >100.4°F (>38°C);
2. Cough, sore throat, or shortness of breath; and
3. History of contact with poultry or domestic birds (e.g., visited a poultry farm, a household raising poultry, or a bird market) or a known or suspected patient with influenza A (H5N1) in an H5N1-affected country within 10 days of symptom onset.

Recommended Laboratory Testing Procedures

The highly pathogenic avian influenza A (H5N1) virus requires Biosafety Level (BSL)-3+ laboratory conditions for certain procedures. CDC recommends that virus isolation studies on respiratory specimens from patients who meet the testing criteria should not be performed unless all BSL-3+ conditions are met. However, clinical specimens can be tested by polymerase chain reaction (PCR) assays by using standard BSL-2 work practices in a Class II biological safety cabinet. CDC has developed real-time PCR protocols, available to public health laboratories, for various respiratory pathogens, including SARS and influenza A and B viruses. In addition, commercially available antigen-detection tests can be used under BSL-2 levels to test for influenza. Although these rapid tests for human influenza also can detect avian influenza A (H5N1) viruses, the sensitivity of these tests is substantially lower than that of virus culture or PCR.

Specimens from persons meeting clinical and epidemiologic indications for testing should be sent to CDC if they test positive for influenza A either by PCR or antigen detection testing, or if PCR assays for influenza are not available locally. CDC also will accept, for follow-up testing, specimens from persons meeting the clinical and epidemiologic indications but testing negative on the rapid tests when PCR assay was not available. Requests for testing by CDC should come through the local public health agency, or the Missouri Department of Health and Senior Services at 573/751-3334 or 751-0633, or at 800/392-0272 (24 hours a day – 7 days a week).

Additional Recommendations Related to Avian Influenza in Asia

CDC advises that travelers to countries in Asia with documented H5N1 outbreaks should avoid poultry farms, contact with animals in live food markets, and any surfaces that appear to be contaminated with feces from poultry or other animals. More information on travel is available from CDC at http://www.cdc.gov/travel. Additional information on influenza viruses and avian influenza is available from CDC at http://www.cdc.gov/flu. Updated information on human infections is available from WHO at http://www.who.int/en.

On February 4, CDC issued an order for an immediate ban on the import of all birds from Cambodia, China (including Hong Kong), Indonesia, Japan, Laos, South Korea, Thailand, and Vietnam. (Additional information on the embargo is available at http://www.cdc.gov/flu/avian/embargo.htm.) Birds from these affected countries potentially can infect humans with influenza A (H5N1). This order complements a similar action taken by the U.S. Department of Agriculture (USDA).

Because of increasing evidence that avian influenza viruses infect humans, persons involved in the slaughter of poultry potentially infected with avian influenza viruses or their contaminated environments should follow WHO recommendations for worker protection, available at http://www.wpro.who.int/avian/docs/recommendations.asp.

Background Information[1,2]

Influenza viruses that infect birds are called "avian influenza viruses." These are type A influenza viruses that are genetically distinguishable from influenza viruses that usually infect people. There are many subtypes of avian influenza A viruses, including H7 and H5. Avian influenza viruses can be distinguished as "low pathogenic" and "high pathogenic" forms based on genetic features of the virus and the severity of the illness they cause in poultry.

Birds that are infected with avian influenza viruses can shed virus in saliva, nasal secretions, and feces. Contact with feces or respiratory secretions is important in the transmission of infection among poultry. Between flocks, infection usually spreads due to movement of infected birds and the actions of humans in moving feedstuff, personnel, equipment, and vehicles into and from premises that are contaminated with infected feces or respiratory secretions. The duration that these viruses can survive in the environment depends on temperature and humidity conditions, but they may survive up to weeks in cooler and moister conditions.

Avian influenza viruses do not usually infect humans; however, since 1997, human infection with avian influenza viruses has been confirmed on five occasions.† The ability of avian viruses to transmit from person to person appears limited.

Antigenic analysis and genetic sequencing distinguish between influenza viruses that usually circulate among birds and those that usually circulate among humans. Sequencing of the H5N1 viruses obtained recently from five persons in Vietnam and Thailand, including one sister from a cluster in Vietnam, has indicated that all of the genes of these viruses are of avian origin. No evidence of genetic reassortment between avian and human influenza viruses has been identified. If reassortment occurs, the likelihood for the H5N1 virus to be transmitted from person to person will increase.

Genetic sequencing of the five human H5N1 isolates from Thailand and Vietnam also indicates that the viruses have genetic characteristics associated with resistance to the influenza antiviral drugs amantadine and rimantadine. Antiviral susceptibility testing confirms this finding. Testing for susceptibility of the H5N1 isolates to the neuraminidase inhibitor oseltamivir has demonstrated the sensitivity of these viruses to the drug; testing to determine susceptibility to the neuraminidase inhibitor zanamavir is under way.

The majority of the human H5N1 cases are apparently associated with direct exposure to infected birds or to surfaces contaminated with excretions from infected birds. A family respiratory illness cluster in Vietnam suggests the possibility of limited person-to-person transmission. However, other possibilities (e.g., transmission through exposure to surfaces contaminated by H5N1-infected poultry feces) cannot be ruled out. Although no evidence for sustained person-to-person transmission of influenza A (H5N1) has been identified, previous experiences with avian influenza viruses suggest that limited person-to-person transmission of the current H5N1 viruses could occur. In addition, influenza viruses have the capacity to change quickly. Continued monitoring for new transmission patterns is an important aspect of the current investigation, and is being undertaken by CDC, WHO, and national health authorities in Asian countries.

Controlling the current outbreaks in Asia is challenging because of the large geographic areas and numbers of affected poultry, and the possibility that infections among wild bird populations might be extensive.

Because the influenza A (H5N1) virus could develop the ability to maintain sustained person-to-person transmission, WHO collaborating centers are working to coordinate vaccine development. Efforts are under way to develop influenza A (H5N1) reference viruses for use in vaccine preparation. Decisions on whether to proceed with vaccine manufacture will depend, in part, on the evolution of the current outbreaks.

†Influenza A (H5N1) in Hong Kong in 1997 and 2003, influenza A (H9N2) in Hong Kong in 1999 and 2003, and influenza A (H7N7) in the Netherlands in 2003.

References:

1. CDC. Outbreaks of avian influenza A (H5N1) in Asia and interim recommendations for evaluation and reporting of suspected cases - United States, 2004. *MMWR* 2004;53(05);97-100. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5305a1.htm
2. CDC. Interim Guidance for Protection of Persons Involved in U.S. Avian Influenza Outbreak Disease Control and Eradication Activities; February 17, 2004. http://www.cdc.gov/flu/avian/pdf/protectionguid.pdf